B. REMARKS

A sequence listing, computer disc, and statement under 37CFR 1.821(f) accompany this response. It is respectfully requested that the sequence listing be inserted into this application between the specification and claims.

Claim 1 stands rejected under 35 U.S.C. 102(b) as being anticipated by Salunke, et al. This rejection is respectfully traversed.

The present invention, as defined broadly in Claim 1, is directed to a method of producing purified papillomavirus virus-like particles. The method comprises (i) purifying disassembled papillomavirus virus-like particles (VLPs), and (ii) reassembling the disassembled papillomavirus-like particles (VLPs) from step (i) to produce purified papillomavirus virus-like particles (VLPs).

Salunke does not disclose or even remotely suggest to one of ordinary skill in the art Applicants' method as claimed. Salunke discloses the expression of the polyomavirus VP_1 capsid protein in *E. coli*. When the expressed VP_1 capsid protein is purified by precipitation at low ionic strength, the protein forms capsomere-like aggregates. At high ionic strength, the capsomeres associate to form capsid-like assemblies and polymorphic aggregates.

Salunke also discloses that polyoma virions are disassociated to the capsomere level with 10 mM EGTA, 3 mM dithiothreitol, and 0.15 M NaCl at a pH of 7.5 or higher. Increasing the salt concentration reduced the extent of dissociation, and in 1 M NaCl the virions are stabilized.

Salunke is directed to the recombinant expression of polyomavirus VP_1 capsid protein, which assembles into polyomavirus capsomeres or capsids, and to the disassembly of polyomarivus virions. Nothing in Salunke discloses or even remotely suggests to one of ordinary skill in the art the production of purified papillomavirus virus-like particles. Therefore, Salunke does not anticipate Applicants' method as claimed nor does Salunke render Applicants' method as claimed obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejection under 35 U.S.C. 102(b) be reconsidered and withdrawn.

With respect to the double patenting rejections, the Examiner is advised that application Serial No. 09/457,594 issued as U.S. Patent No. 6,962,777 on November 8, 2005.

Accompanying this response are terminal disclaimers with respect to the '777 patent, and the '945 and '765 patents cited by the Examiner. It is therefore respectfully requested that the obviousness-type double patenting rejections be reconsidered and withdrawn.

Claim 1 stands rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between steps. This rejection is respectfully traversed.

The Examiner has taken the position that Claim 1 is incomplete in that the steps and conditions that reassemble the disassembled papillomavirus VLPs are missing, such as the removal of the reducing agent.

The Examiner is reminded that Claim 1 defines a method of producing purified papillomavirus virus-like particles (VLPs). Such method includes, as noted hereinabove, the steps of purifying disassembled VLPs, and reassembling the disassembled VLPS. The claimed invention, therefore, is not limited to specific methods of disassembling and reassembling papillomavirus VLPs. Instead, the claimed invention is directed to producing purified papillomavirus VLPs through the disassembly and reassembly of VLPs. The specification, in the sixth paragraph of Page 9, states:

> "It is another object of the invention to provide an improved means of VLP purification by incorporating VLP disassembly /reassembly within the purification process."

Further, the specification states at Page 12 lines 10-12 that the present invention "allows for disassembly of crude mixtures of VLPs, purification of the smaller, soluble VLP components (which is simpler due to their greatly diminished size), followed by reassembly at the desired stage of the purification process".

Still further, Page 22, lines 21-23 state that "When performed in conjunction with purification, VLPs will be extracted from cells, disassembled, purified by conventional techniques, and reassembled at the desired degree of purity."

Applicants then in Example 5 describe in further detail their method of producing purified VLPs. At Page 55, lines 16-22, Applicants state the following:

> "As discussed above, conventional protein purification methods are not optimized for use with protein complexes the size of VLPs (20,000,000 Da, 55nm diam. particles). In particular, the sheer size of the VLPs dramatically lowers the capacity and utility of most chromatographic resins, as much of the reactive chemistry on the resin is sterically

> inaccessible to the VLP. However, this difficulty can potentially be avoided by disassembling crude VLPs extracted from cells purifying the disassembled VLPs using standard methods, and reassembling the VLPs at the desired stage of purity."

Thus, Applicants state clearly in the specification that their claimed method of producing purified papillomavirus VLPs comprises the steps of (i) purifying disassembled VLPs; and (ii) reassembling the disassembled VLPs. Applicants are the first to invent such method. Contrary to the Examiner's assertions, there is no gap between the step of purifying disassmbled VLPs and the step of reassembling the disassembled VLPs.

In the rejection under 35 U.S.C. 112, second paragraph, the Examiner is requesting that Applicants include in Claim 1 the precise conditions that would lead to reassembly of the VLPs, and more particularly that Applicants define the reassembly step in Claim 1 as including the removal of the reducing agent.

Such a request is contrary to the interests of justice. Applicants and only Applicants are the first to discover that one may produce purified papillomavirus VLPs by purifying disassembled VLPs and then reassembling the disassembled VLPs. It would be contrary to the interests of justice to require Applicants to limit the scope of their protection to a specific method of reassembling the disassembled VLPs, and enable one to avoid infringement by devising a method outside the scope of Applicants' claims yet within the scope of Applicants' inventive discovery. For the above reasons and others, Claim 1 is not incomplete and is not unpatentable under 35 U.S.C.112, second paragraph.

With respect to Claim 7, Applicants assert that, contrary to the Examiner's assertion, there is a proper antecedent for the phrase "wherein reassembly . . . reducing agent" as defined in such claim.

Claim 7 depends upon Claim 5. Claim 5, which depends upon Claim 1, defines a preferred embodiment of disassembly of the VLPs.

Claim 7, therefore, depends ultimately upon Claim 1. While Claim 5 does not define any conditions for the reassembly of disassembled VLPs, Claim 1 does include the step of reassembling disassembled VLPs. Therefore, there is antecedent basis for the reassembly of the disassembled VLPs as defined in Claim 7.

For the above reasons and others, Claims 1 and 7 are patentable within the meaning of 35 U.S.C. 112, second paragraph, and it is therefore respectfully requested that the rejection under 35 U.S.C.112, second paragraph be reconsidered and withdrawn.

For the above reasons and others the application is in condition for allowance, and it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,

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